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September 1952

VOLUME VIII NUMBER 9

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CLINICAL PROCEEDINGS

OF THE CHILDRENS HOSPITAL

13th and W Streets, Washington 9, D. C.

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CONTENTS

RETURN TO SENSITIVITIES. *Gordon W. Daisley, Jr., M. D.* 209

CHILDHOOD COMPLICATIONS OF RESPIRATORY ALLERGIES. *William A. Howard, M. D.* 210

DRAMAMINE INTOXICATION. *David A. St. Martin, M. D.* .. 217

CLINICO-PATHOLOGICAL CONFERENCE. *Ruth H. F. Lau, M. D.; Gordon W. Daisley, Jr., M. D., and E. Clarence Rice, M. D.* 219

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RETURN TO SENSITIVITIES

Editorial

When chemotherapeutic and antibiotic drugs were in their infancy, considerable stress was laid by the pioneers on sensitivity tests of the organisms. The purpose, of course, was twofold: to determine whether or not the particular organism was sensitive to the drug, and to see what concentration of drug was needed to deal effectively with the organism.

As the years passed, the need for such tests seemed to disappear. We knew what drugs worked on what organisms, and the commercial supply became so vast and the price so low, that we could give the drugs in massive dosage and know that effective levels had been reached without checking. With the advent of the broad-spectrum antibiotics, even cultures of the organisms except in the most severe infections were neglected, since single or combination administration of them would cover almost all infectious agents. When culture was obtained (as in meningitis or septicemia), simple identification of the organism was enough; routines of treatment had been established, and followed without thought to sensitivity.

We were issued a warning in the early years of this bactericidal era too; widespread, indiscriminate use of these agents would lead to new strains of organisms insensitive to usual dosage or even completely unresponsive to a drug to which it usually succumbed readily. And sporadically we all saw cases in which this was proven to be true.

We may well still be in the every now and then stage; but with pyramiding increase the reports of insensitivity are reaching the literature. In a significant number of cases reported, *Staphylococcus aureus* now is in the majority of cases insensitive to penicillin. In the Children's Hospital during the past winter, five cases of meningitis due to *Hemophilus influenza* were completely insensitive to sulfadiazine; another needed larger than normal doses of chloromycetin for effectiveness. The hospital routine of using sulfadiazine and chloromycetin for this type of meningitis is now always checked with sensitivity tests.

It appears to us that time for routine sensitivity tests has returned. Organisms are no longer behaving themselves with enough regularity to trust to routine measures. Certainly, in the severe cases of infection, we make a plea for culture and sensitivity testing of all; and offer a thought that in the future pneumonias, otites, and the like may be subject also.

Gordon W. Daisley, Jr., M.D.

CHILDHOOD COMPLICATIONS OF RESPIRATORY ALLERGIES

Special Report No. 242

William A. Howard, M.D.

In the literature dealing with the problems of allergy, there are numerous references to the usual complications of the respiratory allergies including sinusitis, bronchitis, bronchopneumonia, bronchiectasis, emphysema, atelectasis, pneumothorax, subcutaneous emphysema, and cor pulmonale. The majority of the conditions arise in conjunction with long-standing asthma with or without an associated nasal allergy, and are much more common in adults than in the young allergic individual. In children there are other complications or associated conditions which are more frequent and more important, but whose significance is often unrecognized. Some of these, discussed below, are common problems in pediatrics, and successful management of them depends upon a recognition of the role of allergy in their pathogenesis.

In the child, allergy of the respiratory system commonly consists of either a perennial allergic rhinitis or asthma, or a combination of both. Typical hayfever is by comparison less common. Allergy of the respiratory system in the child may be considered as a single problem with a common group of causative agents with symptoms characteristic of the area involved.

In children, the principal local effects of allergy on the nasal and bronchial mucosa are increased capillary dilatation and permeability, edema and increased secretory activity. These tissue changes are responsible for the typical symptomatology so well known to pediatricians, including nasal stuffiness, nasal obstruction, post-nasal drip, morning sneezing and nose blowing, nose-rubbing, mouth breathing, snoring, constant clearing of the throat, itching of the nose, and where the bronchial mucosa is involved, persistent cough and paroxysmal respiratory difficulty or asthma. The tissue changes which are responsible for such symptoms cause insufficient aeration in whatever portion of the respiratory tract is involved and may lead to varying degrees of respiratory obstruction.

Wilson[1], in discussing abnormal pulmonary ventilation, classifies the causes under five different major headings as follows:

1. Primary central nervous system disturbance
2. Disturbance in acid-base equilibrium
3. Primary pulmonary pathology (including asthma)

N.B. From the Allergy Clinic, Children's Hospital, Washington, D.C.

4. Defects in circulation directly interfering with ventilation
5. Neuromuscular defects

Chronic nasal obstruction as a cause of abnormal pulmonary ventilation is not sufficiently appreciated, and is not included in the above classification. Four factors have the leading roles in the development of the complications of respiratory allergies of peculiar interest to the pediatricians. There are nasal obstruction, local tissue changes, infection and asthma, any one or all of which may be operative in the individual patient.

1. *Adenoid Facies.* The facial features which are characteristic of this descriptive term are familiar to every physician who has looked at a child with markedly enlarged adenoids which were causing nasal obstruction. However, adenoidal enlargement is by no means the only, or to my mind the chief, cause of the profound changes in the physiognomy. Allergic nasal obstruction, chronic and persistent comes first. The changes in the facial structure are produced by two chief mechanisms. First, there is an increased effort expended in breathing through the partially obstructed nose. Forced inspiration produces depression of the corners of the mouth, flaring of the alae nasae, and a deepening of the naso-labial sulcus. This tends to make the mouth, upper lip and maxilla more prominent and to produce a flattening of the angle between the nose and cheek. Second, because of the persistent swelling and bogginess of the nasal mucosa, the ostia of the maxillary sinuses are partially or completely occluded from time to time, interfering with proper aeration, drainage and growth. In addition, the mucosal lining of the sinuses takes part in the same allergic reaction which is visualized in the nasal mucosa, and which may be demonstrated in the sinus by means of the x-ray. The failure of full growth of the antra produces an even further flattening of the cheeks. Where adenoidal enlargement is the principal cause of such difficulty, improvement may be expected to follow removal of this tissue. If there is an associated allergic rhinitis such operative intervention will produce little or no change in the picture, and there is very likely to be an eventual regrowth of the adenoid tissue.

2. *Malocclusion:* Malocclusion is the natural result in the child of the interference with normal growth and development of the facial bones and maxilla just described. There develops an overbite of varying degree, with marked prominence of the upper incisors and some recession of the lower jaw. In one group of children undergoing orthodontia, 40 per cent were discovered to have chronic nasal allergy as a factor in the development of the anomalous bite. Correction of the nasal difficulty is not sufficient to relieve the malocclusion, but such correction will make the task of the orthodontist much easier.

Case 1. A white male, aged 6 years was referred because of persistent nasal stuffiness since infancy. The mother stated that she could not remember when the child had breathed through his nose. There was no seasonal variation. Nasal discharge was persistent, and was reported to be clear and thin, rather thick or discolored. Sneezing had been frequent earlier but had become less common during the last two years of the illness. Snoring was described as intense. A nocturnal cough was present. Tonsils and adenoids had been removed three years previously with no relief of symptoms. Malocclusion had developed to such an extent that orthodontia had been undertaken six months previously and braces were present when the child was first seen. The mother gave a history of seasonal hay fever.

Examination showed a well developed and well nourished youngster with a typical adenoid facies, the mouth hanging open and the upper jaw prominent. There was flattening of the cheek bones plus depression of the naso-labial sulcus and drooping of the angle of the mouth. The nasal passages were almost completely occluded on both sides by a swollen edematous mucous membrane which was pale and covered with a thin mucoid exudate. The tonsils were out but the posterior pharyngeal wall was studded with small shiny patches of hypertrophied lymphoid tissue. There was a mild cervical adenitis. There were no abnormal chest findings. The rest of the examination was essentially normal.

Laboratory work showed a pronounced eosinophilia of the nasal mucous (approximating 75 per cent of the cells seen) and there was a blood eosinophilia of 8 per cent. Intradermal skin tests showed a marked active (++++) reaction to house dust and a moderate reaction (++) to feathers. There were slight (+) reactions to a few other of the common inhalants but no reactions to pollens or foods.

The mother was given instructions for the preparation and maintenance of the child's room in a state as free from respiratory allergens as possible and for minimizing his contacts with these materials in the rest of his activities. At the same time immunization with a dust and feather extract was begun. Response was prompt and gratifying. Within a few weeks there was considerable clearing of the nasal obstruction and discharge, sleep improved and the cough and snoring lessened. At the end of six months of treatment the child breathed normally through his nose. At this point the orthodontist advised the mother that he was discontinuing braces stating that he could not keep up with the rapid changes taking place in the upper jaw. He suggested instead that after a period of another year of allergy therapy the child should return for correction of the remaining malocclusion. This was subsequently done with quite remarkable changes in the child's physical appearance and mental outlook.

This child does not represent an isolated instance, but is one of a group presenting more or less similar findings. While malocclusion is not necessarily a regular accompaniment of nasal allergy, this child shows quite well the relationship between the two. It is obvious that unless detection and treatment of nasal allergy when it is an underlying cause of malocclusion is undertaken, the task of the orthodontist is made doubly difficult.

3. *Otitis Media and Deafness:* The frequent association of nasal allergy and chronic involvement of the middle ear should be stressed. The anatomy of the nasopharynx makes it quite obvious why either enlarged adenoids or hypertrophied lymphoid tissue from any other cause produces swelling

and obstruction of the ostium of the Eustachian tubes with resultant middle ear difficulty. In the allergic individual, the typical story is that of repeated upper respiratory infections with attacks of middle ear infection, finally with tonsils and adenoids being removed. There follows a period of temporary relief, but where nasal allergy is present the condition usually recurs. In some instances, infection may not be the primary problem but rather, diminished hearing as a result of chronic obstruction of the Eustachian tube on one or both sides. In some individuals, removal of the tonsils and adenoids or application of radium to the nasopharynx or both is productive of prompt relief, while in others relief cannot be obtained by any means until therapy is directed toward the nasal allergy.

4. *Nasal Polyps:* Nasal polyps are neither a very common nor very important complication of nasal allergy in the child. They are mentioned primarily to indicate their allergic etiology. There is considerable evidence to indicate that polyps develop as an advanced response to repeated insults to the nasal mucosa by the offending allergen. Nasal polyps can be shown to disappear with proper allergic therapy without the necessity of operative removal. Polyps may also occur in the paranasal sinuses.

5. *Sinusitis:* I believe that making a diagnosis of sinusitis in a child places a great responsibility on the individual making the diagnosis until he has clarified both the location of involvement and the nature of the etiology. We are all familiar with the loosely used terms of sinobronchitis and bronchosinusitis chest which are often applied to certain children with increased markings in the hilar regions of the lungs and with x-ray changes in the antra and ethmoids. These changes are usually thickening of the lining membranes of the sinuses sometimes to the point of leaving an antrum almost completely opaque with the occasional development of cystic or polypoid changes in the sinus lining. Price[10] in his studies of children with this diagnosis found that a majority of them gave a typical allergic history and showed positive skin test findings. He also found that among definitely allergic children the incidence of sino-bronchitis was much higher than in those children with no allergies.

Continental writers[2] tend to incriminate infection as the usual etiology of sinus disease in children but the symptoms described including lassitude, irritability, school failure, bad complexion, low fevers, adenoid facies, otitis, nocturnal cough and adventitious bronchial sounds, could just as easily be due to nasal and sinus allergy. Goodhill[3], in this, states that by far the commonest variety of sinusitis in childhood is the allergic variety and that no treatment is satisfactory until management of the allergy is included. Grove[4] reporting from Cooke's Clinic in New York believes that in children, tonsils, adenoids and other lymphoid tissue are much more

important from an infection standpoint than are the sinuses, although he claims the reverse is true in adults. Most pediatricians will deny that infectious sinusitis is much of a problem in children with the exception of the ethmoid sinusitis that occurs to some degree with almost any severe upper respiratory infection.

Perhaps more important is the relationship of sinusitis of one kind or another to the persistence of allergic rhinitis of bronchial asthma. There is a definite association but whether the sinusitis is simply one more manifestation of the respiratory allergy or whether the presence of infected sinuses contributes to the persistence of allergic symptoms is not always easily decided. Cooke[5] believes that bacterial allergy plays an important role in the adult and routinely recommends the removal of all foci of infection about the nose and throat, including infected sinus membranes. In children, this picture is not so clear and any treatment of the sinuses should be carefully and thoroughly considered.

6. *Bronchitis:* It is probably not correct to call bronchitis a complication of respiratory allergy, but it occurs so commonly, and the term is so often used in conjunction with asthma that some clarification becomes desirable. Paroxysmal dyspnea or wheezing is so common a finding in the acute pulmonary conditions of infancy and early childhood that the term, asthmatic bronchitis, has very little significance. Most of the wheezings heard in the chests of infants under the age of one year are directly related to bronchiolitis or interstitial pneumonia, and should not be termed asthmatic unless there are other more definite and confirmatory indications of allergy in the child. One conclusion is inescapable, however, and that is that in the older allergic child, infection in the nose, throat, or chest often initiates an attack of asthma. By some this is taken as an indication of bacterial allergy, but most pediatric allergists tend to classify the infection as merely one of the many trigger mechanisms which may set off an attack. Chronic bronchitis is not usual in the respiratory allergies of childhood.

7. *Bronchiectasis:* Respiratory allergy is very often mentioned as a possible etiologic factor in the development of bronchiectasis, but relatively few asthmatics develop this serious complication. Gay[6] believes that it is a rare complication of allergic bronchial asthma, and finds that those patients who do develop bronchiectasis usually have an associated chronic sinusitis. Feinberg[7] believes that some adults develop a mild non-progressive bronchiectasis superimposed on a chronic bronchitis, in which the dilatation and sacculation are mild and cylindrical only. In the child, bronchiectasis is uncommon in even the most severe asthmatics.

Case 2. W. S., a white male aged 9 years, has been a known asthmatic since the age of 3 years. He represents what can only be called a complete failure to obtain

any kind of a therapeutic result regardless of the methods employed. He has been treated by several allergists in different cities to which he has moved. Over the years, regardless of treatment, his attacks have remained just as severe, but less frequent than they were in earlier years. During the first year or two, he required hospitalization once or twice a month; now he is hospitalized about two or three times a year. Between his acute attacks he has a constant exertional wheeze, and usually has a tight, breathless cough. Foci of infection have been removed; immunizing injections of dust and feathers have been given; stock and autogenous bacterial vaccines have been used; elimination diets have been used empirically ; all the antibiotics have been given thorough trials, and finally ACTH and cortisone have been used during an occasional acute episode. On one occasion, cortisone was used over a prolonged period—four weeks—without appreciable benefit. Emphysema and the typically deformed chest have developed. Finally, for the purpose of trying to find some other reason for his difficulty, and to try to make a more accurate prognosis, sinus x-rays were taken and a bronchogram was done. To our surprise and relief, even after six years of almost constant difficulty, the chest shows no evidence of bronchiectasis. Sinus films are reported to show involvement of the maxillary antra as well as the ethmoids. These are difficult to interpret in view of the child's almost complete lack of upper respiratory symptoms. However, a course of x-ray therapy to the sinus area is contemplated as one more effort to relieve this child's symptoms. In answer to the almost automatic question which follows this child's description, I can only say that to date we are unable to find any psychogenic cause for his difficulties. His father is unable to move to Arizona, but it is contemplated that an uncle who lives in that direction may be of some help if his condition remains unsatisfactory.

8. *Emphysema:* The presence of emphysema during the acute attack of asthma, and the eventual development of a chronic asthmatic are well known clinical problems. Mention is made of these problems here only to indicate that they occur in the young asthmatic, and that the pulmonary damage done may be irreversible. This constitutes one of the most valid reasons for making every effort to check the course of allergic asthma in the child by the most expeditious means possible.

9. *Chest deformities:* Three types of chest deformities are recognized in the allergic child. First is the funnel chest deformity which is a simple depression, variable in depth involving mainly the lower portion of the sternum, the xiphoid and the neighboring rib cartilages. It is a frequent finding in chronic nasal obstruction resulting either from nasal allergy or enlarged adenoids. It is one more evidence of the increased effort necessary to inspire through the partially-blocked nose.

The second chest deformity is that which is typical of asthma of long standing. Initially there is noted a more horizontal position of the ribs, and a bunching and overlapping of the rib cartilage attachments to the sternum. Later, the upper part of the chest becomes ballooned out while the lower portion is drawn in and contracted.

Barrel chest, the third type of deformity, is typical of emphysema and is not commonly found in children.

10. *Growth:* No discussion of a chronic disease process in infants and children can be complete without some statement as to the effect of the disease or condition on the child's growth and development. It may be stated that active allergy is a common cause of growth failure, and that control of allergy is usually accompanied by a corresponding growth repair, provided an adequate diet is furnished. Cohen and Abram[8] were able to show these points conclusively on the Wetzel grid. From their data they also indicated that allergy may occur more frequently in children who by inheritance are constitutionally slender.

In conclusion, I should like to quote Dr. Leo Criep[9], who deftly summarizes most of which I have said in a few brief well chosen words:

"As a rule, in spite of wishful thinking and endless temporizing, the untreated allergic child continues to suffer. In this way, untreated nasal allergies become complicated by nasal polyps, the occurrence of nasal infection, and the development of facial and dental deformities; bronchial asthma develops into emphysema, chest deformities (and bronchiectasis). Skin allergies lead to secondary changes such as keratosis and lichenification. The continuation of allergic symptoms for a long period of time affects the child's health, growth, and personality. He loses weight, becomes irritable, fretful, and sleepless. He misses school, cannot play with other children, and frequently finds it difficult to learn a trade which will help him obtain and hold a gainful occupation."

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DRAMAMINE ® INTOXICATION

Case Report No. 243

David A. St. Martin, M.D.

INTRODUCTION

This case is presented because of its striking similarity to atropine intoxication, adding to the large list of toxic substances to which children may have access. A similar case does not appear in the literature.

CASE REPORT

R. G. H., a four and one-half year old white male, was admitted to the Children's Hospital on April 5, 1952. The present illness began approximately five hours prior to admission when it was noted that the patient was tremulous and irrational. He had seemed perfectly well when he awoke. A physician examined the child and recommended hospitalization.

The patient had played with his older sister from the time he awoke until the onset of his illness one and one-half hours later; he had not been observed by either parent during this interval. He had had no recent illness or injury, and had experienced no similar episode previously. There were no known poisons to which the patient had access. The only medicines kept in house were cough syrup, a liniment, and Dramamine ○. The latter drug was used by the patient and his sister for carsickness.

The patient's parents and sister were apparently well. A maternal aunt had convulsions in infancy, but no other member of the family was known to have seizures.

Birth, developmental, and feeding histories were normal. He had chicken pox at age two years and had a tonsillectomy one year ago.

The physical examination revealed a well developed and well nourished white male with a flushed face, dilated pupils, gross tremors, and hyperactive behavior. His temperature was 100.2 F.; the pulse rate was 120; the respiratory rate was 26; and the blood pressure was 120/80. The skin was not remarkably dry. The pupils were equal, round, and measured 5 millimeters; they reacted to sustained light stimulation, returning quickly to their previously dilated state. The fundi were not examined satisfactorily due to the constant darting movements of the eyes. The tongue and oral mucosa were drier than normal. The neck was supple. No abnormality of the cardiorespiratory system was discerned. Examination of the abdomen was negative. Neurologically, the patient was extremely hyperactive, being distracted easily by noises or movements in any portion of the room. He was having visual and questionable auditory hallucinations; he talked incessantly. His gait was staggering. No cranial nerve involvement was apparent. Pain and touch sensation were intact. All the deep tendon reflexes were hyperactive and there was unsustained bilateral ankle clonus.

The tentative diagnosis was atropine intoxication. However, when the parents returned home, they discovered that fifteen 50-milligram tablets of Dramamine were missing; the empty box was found and the sibling saw the patient ingest the tablets.

The patient was observed closely and followed with frequent checks of the vital signs which revealed nothing remarkable. The patient remained hyperactive, con-

N.B. This patient was admitted to the ward service of Dr. Preston A. McLendon

tinued to hallucinate, but within twelve hours after admission he was lucid and otherwise was normal. The patient received no sedation. Complete blood counts on admission and on subsequent days were essentially normal. Routine urinalyses were normal except for one plus acetone on admission and two plus acetone on the following day. The patient was discharged on the third hospital day.

DISCUSSION

In 1949, Gay and Carliner reported the use of Dramamine ® in the prevention and treatment of motion sickness[4]. Since this report, many others have appeared relative to the use of the drug in motion sickness, postoperative vomiting, vomiting of pregnancy, radiation sickness, and adversive syndrome.

Dramamine ® (*Searle*) is the trade name for 2-(benzohydryloxy)-N,N-dimethylethylamine 8-chlorotheophyllinate, an antihistamine. It is closely related to diphenhydramine (Benadryl—*Parke Davis*) which is the benzhydryl ether of dimethylaminoethane. To overcome the principle side reaction of the antihistamines—drowsiness—the theophylline group was added to Benadryl to act as a stimulant; 8-chlorotheophylline combines chemically with Benadryl to form Dramamine®[3].

Various side effects of the antihistamines other than drowsiness include fatigue, nausea, vomiting, dizziness, headache, dryness of the mouth, nervousness, diarrhea insommia, toxic eruption, dysuria, convulsions, and anemia[1, 2, 5, 8]. By virtue of their local anesthetic, quinidine-like, and anti-acetylcholine effects, the antihistamines belong to a large group of substances which have these actions in common, including antispasmodics, analgesics, local anesthetics, and atropine-like substances[6].

The adult dose of Dramamine ® should not exceed 400 milligrams per day[7]. The patient in this case had 750 milligrams as a single dose. It is known that theophylline is a central nervous system stimulant, and that diphenhydramine can cause convulsions in animals[9]. Too, it is known that the antihistamines have an atropine-like effect. Thus, the grounds for this patient's clinical picture of hyperexcitability, flushed face, dilated pupils, and dry mouth which so closely mimicked atropine poisoning can be inferred.

SUMMARY

A case of Dramamine ® intoxication has been presented which mimicked atropine poisoning.

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CLINICO-PATHOLOGICAL CONFERENCE

Directed by: E. Clarence Rice, M.D.
Assisted by: Ruth H. F. Lau, M.D.
By invitation: Gordon W. Daisley, Jr., M.D.

Ruth H. F. Lau, M.D.

This white female infant was admitted to The Children's Hospital 48 hours after birth and died on the seventh day of life.

The prenatal history was essentially normal and the labor lasted for four hours. Delivery was vertex and spontaneous; birth weight was 5 pounds and 9 ounces.

Shortly after birth it was noted that this infant produced a large volume of oral mucous. Breast feeding was not attempted, but water was given by mouth during the first 24 hours, resulting in regurgitation; these episodes being associated with cyanosis and coughing. The patient was seen at this time by a pediatrician, who attempted to pass a small nasal catheter, but this was blocked at the level of about six inches from the nares. Vigorous attempts to further the passage into the stomach were not possible. A tentative diagnosis of tracheo-esophageal fistula with esophageal atresia was made and the child was referred to Children's Hospital immediately.

On admission, an attempt at oral intubation was again made and a definite block was met, which was thought to be present in the upper third of the esophagus. A small volume of lipiodol was introduced into the nasal tube, by which a distinct pouch was outlined at the bifurcation of the trachea. A second attempt of intubation, however, succeeded in passing the tube into the stomach which was markedly distended by air. At this point it was thought that the esophagus was patent, but a possible tracheo-esophageal fistula did exist. Physical examination after the patient was admitted to the ward was essentially negative except for the above.

Milk formula was offered, resulting in prompt regurgitation through the nose and mouth. Examination of the chest at this time revealed bilateral rhonchi which disappeared after aspiration. The child was then maintained on intravenous fluids and whole blood. On the second hospital day, another attempt at esophageal intubation again demonstrated an obstruction in the

upper segment of the esophagus. Lipiodol was injected into the tube, but prompt regurgitation again resulted. Esophagoscopy was able to demonstrate a short, patent esophageal segment, but further visualization was impossible. Bilateral infiltrative processes in the lung appeared in the x-ray on the third hospital day during which time oral fluid still could not be administered. A two-stage gastrostomy was done on the third and fourth hospital day to relieve the gaseous tension and the infant withstood these operative procedures well. Fluid given through the gastrostomy wound produced regurgitation through the nose and mouth. Each of these episodes was accompanied by intense cyanosis. Examination of the chest at this time revealed numerous fine rales throughout the lung fields. Oxygen, continuous intravenous fluid, and constant suction failed to improve the patient's condition which was definitely downhill. Regurgitation of frothy fluid occurred frequently. Respiration became more irregular and the infant expired on the seventh day of life.

DISCUSSION

Gordon W. Daisley, Jr., M.D.: The differential diagnosis of gastrointestinal and respiratory difficulty in the newborn period is not extensive and it should be a relatively easy matter to arrive at a definite conclusion. The symptoms outlined in the protocol suggest the following six diagnoses:

1. *Simple aspiration.* It is not infrequent with the first feeding for regurgitation to occur and if any of the material is aspirated; coughing and cyanosis may well be associated. The respiratory distress may continue particularly if atelectasis and/or bronchopneumonia ensue and further feedings may increase the infant's difficulty usually because the respiratory tract is further diminished by the presence of food in the mouth. Such a diagnosis is difficult to entertain in this instance because of the repeated attacks associated with feedings, and the relative lack of symptoms otherwise.

2. *Vascular-ring anomalies.* Another cause of both respiratory and gastrointestinal difficulty which is extrinsic to both systems is double aortic arch or other vascular-ring anomaly. Although they rarely cause symptoms in the immediate neonatal period, such anomalies can have a sufficiently tight ring to cause embarrassment from birth. The usual symptoms are hoarseness, crowing respiration, and impaired deglutition, and not the severe symptoms illustrated in this case. This diagnosis would have to be entertained until the x-ray showed the opaque substance to end in a blind pouch following the esophageal swallow. I have never known of a ring which was so tight as to cause complete stricture of the esophagus.

3. *Tumors of the Mediastinum.* Causing symptoms in much the same

way as the ring anomalies, tumors of the mediastinum could encroach upon the lumena of both the trachea and esophagus. The chest x-rays rule this out as the etiologic agent; a tumor large enough to cause severe symptoms is large enough to be seen.

4. *Diaphragmatic hernia.* Defects in the diaphragm are not always demonstrable in an upright film in an infant, and they are capable of causing the symptomatology exhibited here. To cause continual respiratory and gastrointestinal distress, however, it is likely that the bowel would have to stay herniated into the chest cavity. Certainly, the opaque material should pass into the stomach after its ingestion, and there should be later evidence of it in the intestinal tract in the chest.

5. *Atresias of the lower gastrointestinal tract.* When examining a newborn infant who has vomited and shows respiratory distress, one must also think of atresia in the gastrointestinal tract, with aspiration of vomitus. If the block is in the lower intestinal tract, signs of intestinal obstruction may not be evident immediately, and while a flat plate of the abdomen may show no air below the point of obstruction, this may be difficult to interpret in the first few hours of life. The dilatation of the stomach in this case would make this diagnosis plausible, but the subsequent course of the infant, without signs of intestinal obstruction becoming evident, rules out any such atresia.

6. *Tracheo-esophageal fistula with esophageal atresia.* While all of the above diagnoses would have to be entertained until studies or the subsequent course of the infant proved or disproved them, none of them satisfies me as to the diagnosis. We are left then with the consideration of tracheo-esophageal fistula, and indeed that was the clinical impression, an impression which I am sure was correct. The history of excessive mucus with following regurgitation of feedings associated with cyanosis and respiratory belaborment is the classic textbook picture. The confirmation of the esophagus ending in a blind pouch when given an opaque substance to swallow was established. The clinicians were disturbed, however, when a soft rubber catheter was passed into the stomach on one occasion and there was an x-ray to prove its presence there. Unfortunately, a lateral film was not obtained at the same time.

There are four anatomical types of tracheo-esophageal fistula, and over 80 per cent of them have the distal end of the esophagus continuous with the bifurcation of the trachea. I believe that the one time that the catheter was passed into the stomach, the tube entered the trachea and went out the distal segment of the esophagus which communicated to the trachea. This could have been confirmed on a lateral film. If such an impression is correct, the air in the stomach could be explained on this basis, rather

than a patent alimentary tract. Certainly, at all other times the tube seemed to encounter the blind pouch.

Those following the case must have felt that was the answer, for they performed a gastrostomy after some delay. The subsequent regurgitation of the material put into the stomach accompanied by severe respiratory difficulty is added proof, for if the surgery did not include tying off the distal end of the esophagus, the infant would have drowned in the fluids given, and unfortunately such seemed to be the case. If the distal end was tied off, then some other factor must have caused the demise.

In summary then, it seems that this patient had a traceho-esophageal fistula with esophageal atresia in which the clinicians were temporarily misled when a catheter was passed into the stomach, through the trachea and the distal end of the esophagus rather than through a patent esophagus. Delay in recognition of the condition evidently made the surgeons feel that attempting a direct anastamosis of the segments, the choice of treatment today, was too dangerous, and they temporized by doing a gastrostomy. Delay in performing the gastrostomy and failure to tie off the distal end of the esophagus lead to the infant's death, as the fluids introduced into the stomach were regurgitated into the trachea and aspirated into the lungs.

POST MORTEM FINDINGS

Ruth H. F. Lau, M.D.: The main pathology in this case was found in the thoracic cavity and consisted of a tracheo-esophageal fistula of a common variety. The upper segment of the esophagus was normal to the level of the bifurcation of the trachea where it ended in a blind pouch. This segment was adherent to, but did not communicate with the trachea. The lower third of the esophagus was of normal caliber, but the middle third of the tube became progressively more narrow and on approaching the level of the bifurcation of the trachea, it was adherent to the posterior surface of the trachea and was represented only by a fibrous cord. There was no communication between the dilated pouch of the upper esophagus and the lower segment. There was a fistulous communication between the lower esophageal segment and the trachea. On opening the trachea, the communication between it and the lower portion of the esophagus measured 0.3 centimeters.

The lungs were about twice the normal weight. Grossly, they were markedly congested and showed infiltration and early abscess formation. Microscopically there was diffuse involvement because of the aspiration of food and mucus that had occurred, the typical microscopic picture of aspiration pneumonitis being present.

Other organs showed only congestive changes.

PATHOLOGIC DISCUSSION

E. Clarence Rice, M.D.: During the past twelve to fourteen years there has been a constant revision in the frequency of occurrence of certain causes of death in patients of the pediatric age group due to the reduced number of deaths from infection. This change brings into focus new leading causes of death, viz., malignant tumors and leukemia and developmental anomalies. Because of improving operative technique, the use of antibiotics and the availability of adequate means of maintaining fluid and electrolyte balance, it is becoming possible for the surgeon and pediatrician to salvage an increasing number of these patients, who formerly were considered to be without benefit of surgery. To profit by these advances, the pediatrician must be on the alert and make his diagnoses early if he wishes to avoid complications which may make operation impossible or its successful outcome unlikely. Developmental anomalies of the digestive and respiratory tracts are among those which require prompt recognition and surgical intervention.

Atresia of the esophagus combined with tracheo-esophageal fistula brings up interesting theories as to its causation. One which is widely considered to be the cause explains the defect as being due to delay of the process whereby "the respiratory anlage is separated from the digestive tube and to a consecutive process whereby part of the esophagus is incorporated into the posterior wall of the trachea[1]." Fluss and Poppen[2] bring up the interesting possibility that vascular anomalies can and do give rise to these defects in the trachea and esophagus.

With this patient, the ability of the physician to pass a tube from the mouth down into the stomach could certainly confuse him as well as aid him in making a correct diagnosis when contrast media was used.

Swenson's[3] report of 113 cases operated on with 57 of the patients surviving is an example of the benefits which are being achieved from present-day surgery supplemented by adequate pediatric care.

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